

Operative Classification of Brain Arteriovenous Malformation

Part Two: Validation

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Key Words: arteriovenous malformations, brain, treatment

Summary

The most important issue when dealing with a patient with a brain AVM is the decision whether to treat or not. Only after this decision has been made, taking into consideration a number of factors depending on both the patient and the specific type of AVM, can the best option for treatment be chosen.

An operative classification of brain AVMs, previously adopted in the Department of Neuro-radiology and Neurosurgery of Verona (Italy) and published in this journal, was subjected to validation in a consecutive group of 104 patients clinically followed for at least three years after completion of treatment.

This classification, slightly modified from the original version concerning the importance of some specific items, allowed us to assess the indication to treat in each case, whatever type of treatment was offered to the patient.

Introduction

Brain arteriovenous malformations (AVMs) are complex pathologies. Neither the real pathophysiology nor the risk associated with these intriguing lesions have yet been fully clarified¹⁻³ so that not infrequently the correct therapeutic management for an individual patient may be cumbersome⁴.

The decision to treat a patient or not and, secondly, to select the best options for treat-

ment must take a number of factors into consideration depending on both the patient and the specific type of AVM.

Thanks to the development of modern catheter angiography and MR techniques, over the years a number of classification systems have been proposed and refined^{5,6}.

The different classifications proposed have considered various angio-architectural features such as size, site, number and distribution of afferent vessels, patterns of venous drainage, flow velocity and the amount of blood steal to the adjacent normal brain tissue in order to obtain a possible association with the bleeding risk⁷⁻¹⁴. Nevertheless, the available classifications are so different that comparisons between various series are extremely difficult.

Most relevant papers dealing with predictors of unfavourable outcome identified separately several factors for surgery¹⁵⁻¹⁷, radiosurgery¹⁸⁻²¹ or embolization²²⁻²⁶. In the case of endovascular treatment adverse factors linked to neurological complications were identified by means of clinical characteristics such as age or the absence of pre-treatment neurological deficits²² or morphological AVM characteristics such as deep venous drainage and the size of the AVM²⁵, basal ganglia location²⁴, eloquent areas or fistula²³.

Other adverse factors identified such as periprocedural hemorrhage²⁵, venous deposition of glue²³ or number of embolizations²², do not appear useful for pre-treatment identification of possible risks.

Moreover, in literature morbi/mortality rates deal exclusively with a single type of treatment, scarcely considering the overall rate on completion (i.e. obliteration of the AVM) of combined treatments.

Relying on the data available in literature and on the opinions gained from our personal experience, we developed an operative classification of brain AVMs published in this journal²⁷ with the main aim of helping the physician and the patient to reach informed consent on the treatability of his/her AVM. This classification was mainly based on a thorough review of

the literature and partly on the authors' personal experience, but did not include a review of their own AVM cases.

The main purpose of the present study was to validate and/or refine our previous classification on the basis of the retrospective analysis of 104 patients treated in our institution.

Our Department has developed and utilized a cumulative score (CS) made up of the sum of an intention to treat score (ITS) and a treatment risk score (TRS)^{27,28}. Even though these scores combine morphological AVM features with clinical/physiological factors, their use can be justified by the achievement of a single score, the "core" of the process of decision-making for the single patient (treatment or abstention, type of treatment). Lower ITS scores indicate the need for treatment due to an unfavourable natural history, while lower TRS scores indicate lower risk levels for each type of treatment.

In our previous classification, ITS was made up of the sum of scores deriving from both patient and AVM characteristics. Patient characteristics and relative score were: age (≥ 65 : 2; $\geq 50 < 65$: 1; < 50 : 0); history of hemorrhage (no: 2; yes: 0); neurological deficits not related to a previous hemorrhage (no: 1; yes: 0); patient's firm intention to be treated, important from a psychological point of view (no: 1; yes: 0).

AVM characteristics were: small size, i.e. volume less than 10 ml (no: 1; yes: 0); deep brain location (no: 1; yes: 0); exclusive deep venous drainage (no: 2; yes: 0); associated aneurysms or varix (no: 2; yes: 0). By totalling the patient score (0-6) and the AVM characteristics score (0-6), ITS was calculated ranging from 0 to 12.

For each brain AVM to be treated, TRS ranging from 1 to 5 was calculated, irrespective of the choice of surgery, radiosurgery, embolization or combined treatment. In our Department the decision on which option would be most suitable for the patient is made after assessment by all members of the AVM team. In addition, the patient's preference, which is of no less importance, is taken into consideration.

The most popular grading scheme for predicting surgical risk is the system described by Spetzler and Martin in 1986¹⁶ which divides patients into five risk categories on the basis of three AVM features: size (1-3), eloquence of location (0,1) and pattern of venous drainage (0,1). The grade of any particular lesion is the sum of its score for each of these three charac-

Table 1

Modified Rankin Outcome Scale TOTAL (0-6)	
Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead
ROS 0-2 are considered Independent, ROS 3-6 are considered disabled.	

Table 2 Brain AVMs treated in the Department of Neurosurgery of Verona (period 1998-2005)

Treatment Modality	N° of Patients	Percentage of Total
Direct surgery	27	26%
Direct radiosurgery	29	28%
Embolization	4	3.5%
Embolization + radiosurgery	15	42.5%
Embolization + surgery	24	
Embolization + radiosurgery + surgery	5	
Total	104	100%

teristics, ranging from grade I (simplest and lowest risk) to grade V (most complex and highest risk). Using this classification, permanent morbidity and mortality ranged from 0 for patients with grade I AVMs to 17% for grade V AVMs¹⁵. As in the grading scheme of Spetzler and Martin, by far the most popular and widely accepted, two other grading schemes scoring 1 to 5 both for radiosurgery and embolization are used respectively in our institution.

The main feature in predicting radiosurgical risk both for radionecrosis and/or failure of treatment is the volume of the AVM nidus. On the other hand, in our experience based on more than 250 treated AVMs^{18,19}, reduced nidus flow (both spontaneous or decreased by embolization) is associated with a higher post-RS obliteration rate, also occurring in a shorter time. After analyzing the results of our personal experience, we assigned a higher score to the larger AVMs (<5 cm³: 1; >5 <10 cm³: 2; >10 <20 cm³: 3; >20 <30 cm³: 4; >30 cm³: 5). One point is subtracted if the AVM has a low flow (for example: a 13 cm³ AVM is scored 2 – not 3 – if it is a low-flow AVM).

In our experience²⁸, the three main factors predicting embolization risk were: volume (<10 cm³: 1; > 10 < 20 cm³: 2; >20 cm³: 3), eloquence (not eloquent: 0; eloquent: 1) and the presence of perforators as feeders (no perforators: 0; perforators: 1).

The cumulative score (CS) was calculated ac-

cording to the total ITS (0-12) and TRS (1-5) scores- According to this procedure, with a score from 1 to 10, treatment was highly recommended, with a score from 11 to 12 treatment was offered but with a significant risk and with a score from 13 to 17 no treatment at all was advised.

Materials and Methods

104 patients with brain AVMs treated in the Department of Neuroradiology and Neurosurgery of Verona University Hospital from 1998 to 2005 were retrospectively analyzed.

The main goal was to verify - and/or improve - the predictive potential of our proposed classification²⁷ which considered both the specific clinical features of a patient together with an individual AVM and the risk associated with the specific morphology of that AVM. After weighing up these factors, we devised a classification system yielding an individual score, tailored for every single patient.

This approach was based mainly on a thorough review of the literature and partly on personal experience derived from our opinions built up over more than 15 years of daily involvement in the field of brain AVMs.

The 104 patients included in the study represent a subgroup of the whole series of patients treated in the same period, fulfilling precise criteria of homogeneity for the following reasons:

Table 3 Mortality and morbidity rates according to type of treatment.

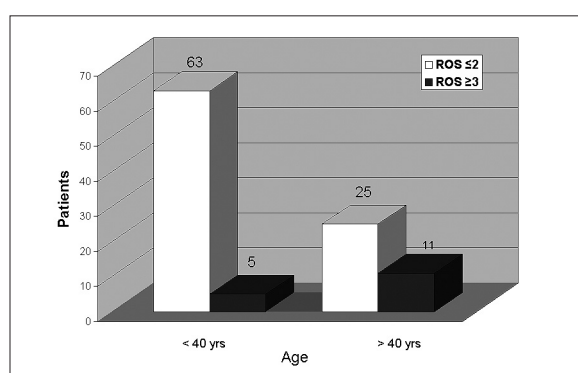
	Direct surgery	Direct radiosurgery	Embolization + Combined treat	Total
Mortality (ROS 6)	1/27 (3.7%)	0/29	0/48	1/104 (0.9%)
Morbidity (ROS 3-5)	5/27 (18.5%)	4/29(14%)	6/48 (12.5%)	15/104 (14%)

Table 4 Distribution of Cumulative Score (CS) among 104 treated patients.

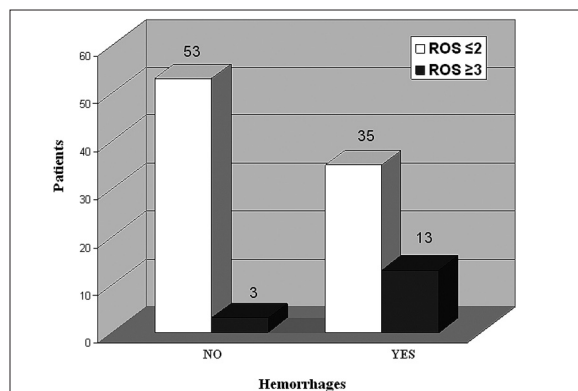
Cumulative Score	PATIENTS			
	Total	Surgery	Radio-surgery	Embo & Combined
1 – 10 Treatment Recommended	99	27	29	43
11 – 12 Treatment Offered With Significant Risk	5	-	-	5
13 – 17 Treatment Not Recommended	0	-	-	-

- all patients had complete clinical/radiological documentation
 - all patients had an adequate clinical/radiological follow-up of at least three years after treatment (mean four years)
 - all patients were treated in a similar manner (same neurosurgical/endovascular/ radiosurgical team; same devices; same materials).
- Morphological characteristics of all AVMs

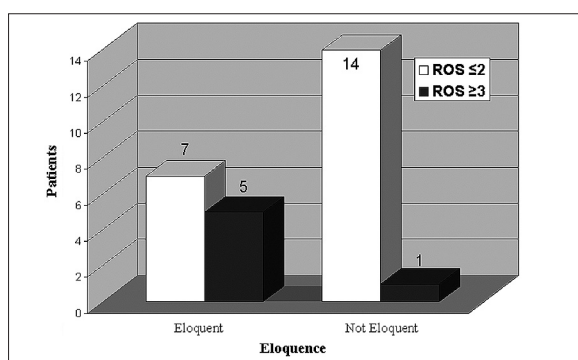
Graph I Distribution of ROS according to age.



Graph II Distribution of ROS according to previous hemorrhages.



Graph III Distribution of ROS according to eloquent/non eloquent adjacent brain.



were evaluated by means of MR and angiographic data, and in particular the precise topography of each lesion was assessed on MR scans while the exact volume was calculated on angiographic films taking into account the magnification factor, using the system described by Pasqualin et Al.²⁹

A modified ranking outcome score (ROS) was used³⁰ for the precise evaluation of neurological disability (Table 1): compared with the original version characterized by a score 0 to 5 according to increasing severity, the modified version includes the score 6 in the event of patient death.

Patients were classified as non autonomous when ROS ranged from 3 to 6 (score 6, death, was included); they were classified as autonomous (ROS ≤ 2) when they were able to work and to carry out a majority of tasks.

Results

In the 104 patients treated, 29 were treated by direct radiosurgery, 27 by direct surgery, four by embolization alone and 44 by combined treatment in which embolization was followed by surgery (24), radiosurgery (15), or both (5) (Table 2).

In the 104 treated patients complete obliteration of the lesion was achieved in 103 (99%). In one patient treated by radiosurgery the AVM was found to be incompletely obliterated (70%) at three year follow-up.

In the group of 104, 16 patients with a ROS score 3-6 were distributed as follows: seven patients with a ROS score of 3, eight patients with ROS 4 and one patient with ROS 6 (deceased). Therefore global mortality was 0.9 % and global morbidity was 14% (Table 3).

As regards distribution according to the type of treatment (Table 3), direct surgery resulted in a mortality rate of 3.7% (1/27 patients) and a 18.5% morbidity rate (5/27 patients). The deceased patient was the oldest of the entire series, was admitted to hospital with a bleeding small left temporal AVM and the cause of death must be attributed to pulmonary embolism. All five of the non autonomous patients treated by direct surgery were admitted to hospital with intracerebral hematoma and their clinical condition was poor.

Radiosurgery, performed in small volume AVMs (<5 ml), did not result in any mortality, with a morbidity rate of 14% (4/29 patients).

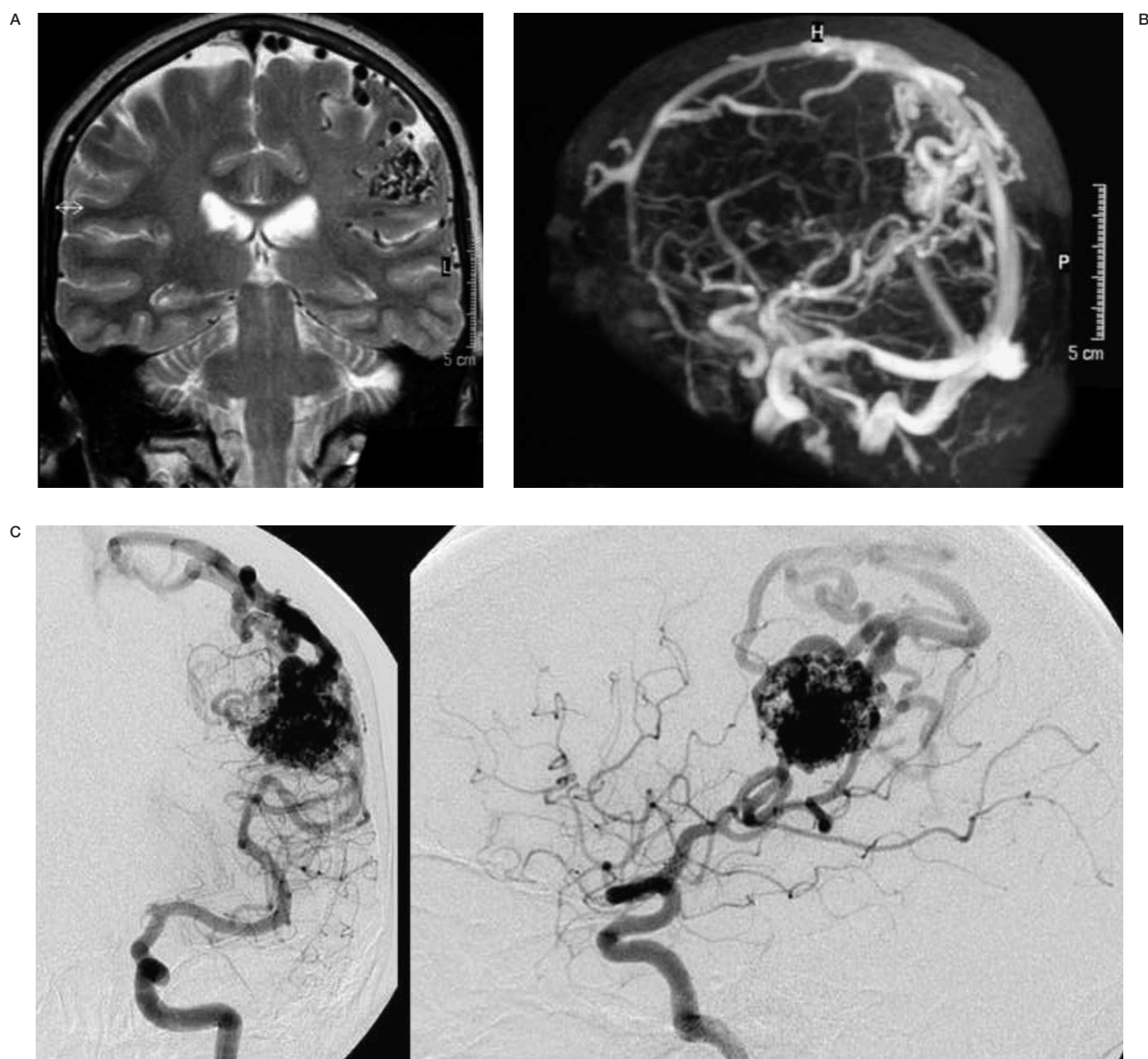


Figure 1 A 52-year-old woman with epileptic seizures. Left parietal post-central 5 ml AVM. ITS= 9 (Age $\geq 40 \leq 60$ yrs = 1; Previous hemorrhages NO = 1; Neurological deficits NO = 1; Firm patient willing YES = 0; Deep brain location NO = 1; Exclusive deep venous drainage NO = 2; Associated aneurysm/varix NO = 2), TRS embolization = 2 (Volume < 10 ml = 1; Eloquence YES = 1; Perforators NO = 0; Unfavourable angio-architecture NO = 0). CS 9+2 = 11. A) Pre-embolization coronal T2-weighted image. B) Pre-embolization left parasagittal MIP reconstruction from 2D-TOF MRA. C) Pre-embolization AP and LL angiography. D) AP and LL angiography after second embolization session. E) CT scan after second embolization. F) AP and LL view two and a half years after radiosurgery and three years after first embolization.

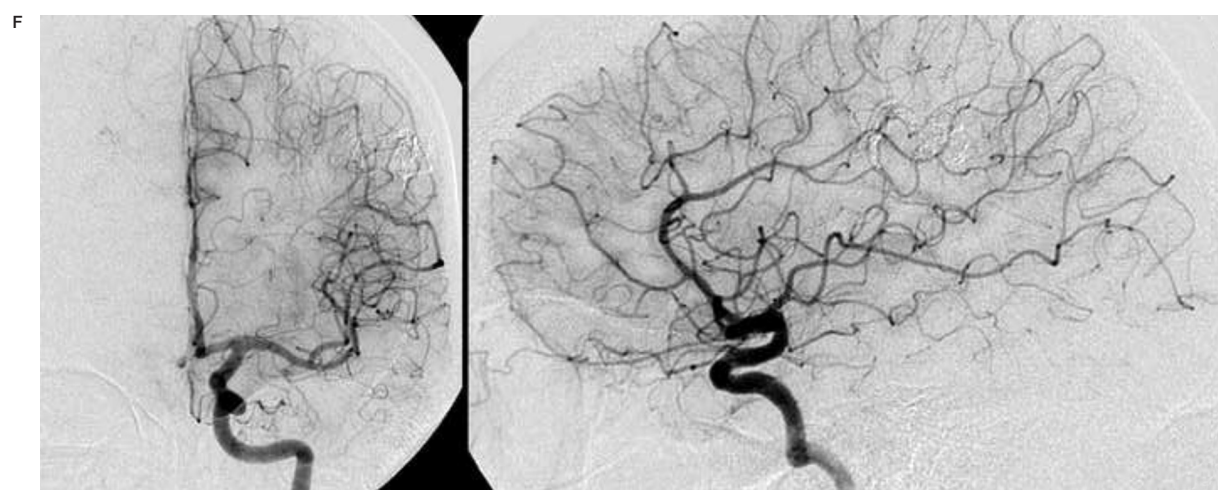
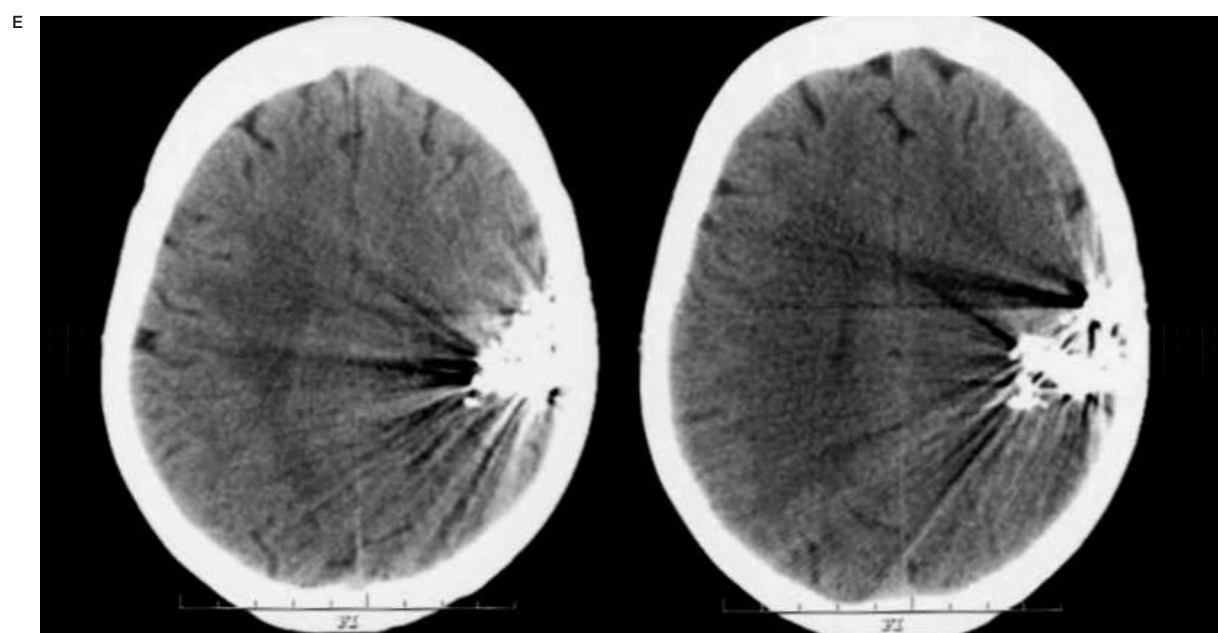
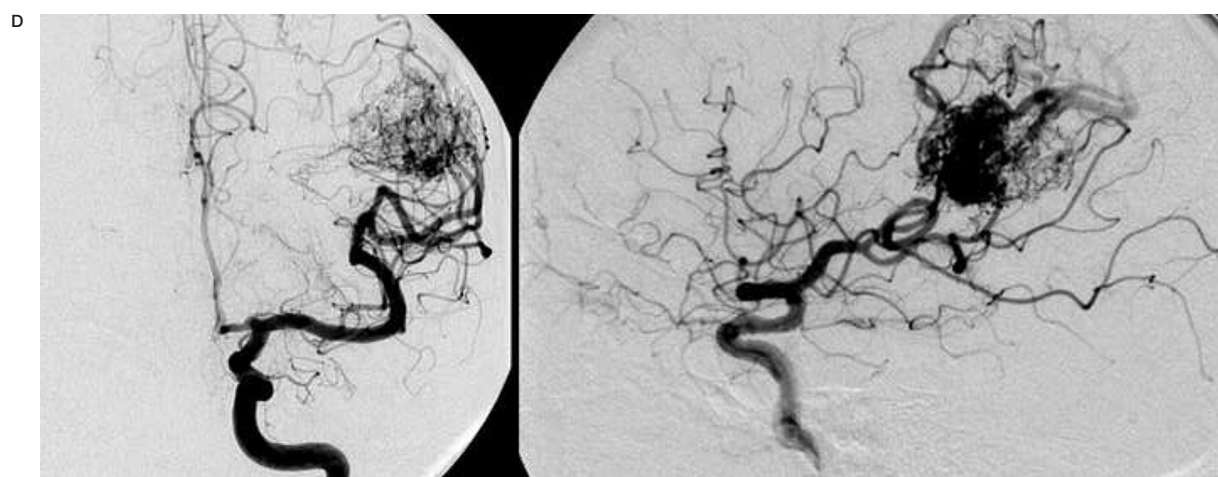
Embolization alone or followed by surgery or radiosurgery did not result in any fatality and presented a morbidity rate of 12.5% (6/48 patients).

To sum up, while the only death was due to surgery, as far as mortality rates are concerned there was no statistical difference between the various types of treatments.

Each item of the intention to treat score was analyzed on the basis of the recorded data (Table 4):

- AGE was a predictor of unfavourable outcome by univariate analysis: older patients (> 40 yrs) were more likely to show significant neurological deficits (ROS ≥ 3 ; Graph I).

Younger patients (< 40 yrs) had a more fa-



avourable outcome (63/88, 72%, were autonomous patients vs 5/16, 31%, non autonomous patients) than older patients (25/88, 28%, were autonomous vs 11/16, 63%, non autonomous).

We concluded that the division into three subgroups adopted in the previous version of the classification works better when the three subgroups are distributed as follows: ≥ 60 yrs, $\geq 40 < 60$ yrs, < 40 yrs, as a higher statistical significance ($p < 0,001$) is reached.

- *Previous hemorrhage* was a predictor of unfavourable outcome by univariate analysis ($p < 0,001$): hemorrhages were recorded in 13/16, 81% of the non autonomous (ROS ≥ 3) patients vs 35/88, 40% of the autonomous (ROS ≤ 2) patients. No previous hemorrhages were recorded for 53/88, 60% of the autonomous patients vs. 3/16, 19% of the non autonomous patients (Graph II).

- *Firm intention of the patient to be treated* was a factor which cannot be considered in our retrospective evaluation but, in our opinion, is of paramount importance in the prospective evaluation of the complex process of decision-making shared by the patient and his/her relatives.

- The remaining items (neurological deficits, small size, exclusive deep venous drainage, associated aneurysm or varix), did not reach statistical significance, even if their importance is evident in current literature.

The factors contributing to the treatment risk score (TRS) were all considered separately as regards surgery, radiosurgery and embolization. All the items evaluated for surgery, (eloquence of adjacent brain, size, pattern of venous drainage) radiosurgery (volume) and embolization (eloquence of adjacent brain, volume, presence of perforating arteries as feed-

Table 5 (A,B) **Brain AVMs intention to treat score (ITS: 0-12)**

A) Patient features (0-6)

		Score
Age (yrs)	≥ 60	2
	$\geq 40 < 60$	1
	< 40	0
Previous hemorrhages	No	2
	Yes	0
Neurological deficits	No	1
	Yes	0
Patient's firm intention to be treated	No	1
	Yes	0

B) AVM characteristics (0-6)

		Score
Small size	No	1
	Yes	0
Deep brain Location	No	1
	Yes	0
Exclusive deep Venous drainage	No	2
	Yes	0
Associated Aneurysm/Variz	No	2
	Yes	0

ers, unfavourable angio-architecture) were considered important, even if they did not reach statistical significance. The only exception was the eloquence of adjacent brain which was significant by univariate analysis for surgery ($p < 0.05$). There were 14/21 (67%) autonomous pa-

Table 6 **BRAIN AVMs Treatment Risk Score (TRS: 1-5).**

A) Surgery (1-5)			B) Radiosurgery (1-5)		C) Embolization (1-5)		
SPETZLER-MARTIN Modified	Grade	Score	Volume cm ³	Score	Volume cm ³		Score
	I	1	< 5	1		< 10	1
	II	2	$> 5 < 10$	2		$> 10 < 20$	2
	III	3	$> 10 < 20$	3	Eloquence	> 20	3
	IV	4	$> 20 < 30$	4		No	0
	V	5	> 30	5		Yes	1
			One point minus if low flow		Perforators	No	0
						Yes	1

tients with an AVM not adjacent to eloquent brain vs 7/22 (33%) patients with an AVM adjacent to eloquent brain. On the other hand, there were 1/6 (17%) non autonomous patients with an AVM not adjacent to eloquent brain vs 5/6 (83%) patients with an AVM adjacent to eloquent brain (Graph III).

As regards CS score, all patients had a score below 12 whatever treatment was selected (score 1-10: 99 patients; Score 11-12: five patients) (Table 4).

This means that the CS score formula, based on personal experience and literature data, was accurate enough to allow an adequate decision for treatment to be made in all the cases: no patient, even if evaluated retrospectively, scored more than 12, in which case treatment would not have been recommended.

Mean ITS was 5, TRS was 2.1 and CS was 7.1. There were small differences between the two groups of patients (autonomous and non autonomous) not reaching statistical significance.

This is not surprising since all the patients were actually considered treatable by our brain vascular team. The CS must be considered an important factor in the decision whether to treat a patient or not. On the other hand, the outcome may not be strictly correlated to CS since other variables (i.e. complications following surgery or anesthesia) may be more important than the patient and AVM features.

Conclusions

As regards the decision to proceed or abstain from treatment, our operative classification was efficient enough for us to verify that the advice for treatment was justified, as none of the patients had a CS score above 12 (the maximum limit for patient treatability). Among the 104 patients treated, only five had a score above 10 (treatment offered although at a significant risk); in all these patients embolization

was performed as the first treatment to decrease the risks associated with surgery and radiosurgery (Figure 1).

As regards the items taken into consideration for the ITS score, age and the presence or absence of previous hemorrhages were statistically significant also as independent factors, thus justifying the higher score attributed. As far as age is concerned, data obtained by the retrospective analysis of our 104 patients suggest the previous subdivisions should be modified. Considering that the two main subgroups of patients belonged to the age groups <40 or ≥40 and that only a few patients were over 60, the new age subdivisions are as follows: <40 (score 0); ≥40 < 60 (score 1); ≥60 (score 2).

Previous TRS, in our opinion, cannot be improved further, as all the items considered proved to be adequate, given that "eloquence of adjacent brain" was statistically significant.

Our attitude is based on a "soft" approach to AVMs at risk, without the aim of achieving 100% occlusion of these malformations by embolization alone. This is justified by the relative low global morbidity/mortality rates in our cases in comparison with other series³¹. Our morbidity and mortality rates refer to a group of patients in which various treatments (mainly combined ones) achieved a near 100% obliteration of the AVM.

In conclusion, our classification (Tables 5 and 6) proved simple and efficient even though it includes many different parameters that were validated on the basis of a retrospective analysis of a significant number of treated patients.

Since the beginning of 2008 this classification has been adopted as a routine protocol for the brain AVMs team in our Department to assess the indication to treat in every single case, whatever type of treatment is offered to the patient.

Data collected from the prospective application of this classification may be useful in the future for its further validation.

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